

What is claimed is:

5 1. A method for ligating a first oligopeptide with a second oligopeptide end to end for producing an oligopeptide product, the method comprising the following steps:

10 Step A: admixing the first and second oligopeptides in a reaction solution including a catalytic thiol, the first oligopeptide including a C-terminal thioester, the second oligopeptide including an N-terminal cysteine having an unoxidized sulphydryl side chain; then

15 Step B: condensing the unoxidized sulphydryl side chain of the N-terminal cysteine with the C-terminal thioester for producing an intermediate oligopeptide linking the first and second oligopeptides with a β -aminothioester bond; and then

20 Step C: rearranging the β -aminothioester bond of the intermediate oligopeptide of said Step B for producing the oligopeptide product linking the first and second oligopeptides with an amide bond.

25 2. A method as described in Claim 1 wherein, in said step A, the catalytic thiol is selected from the group consisting of unconjugated mercaptans and conjugated thiols.

30 3. A method as described in Claim 2 wherein, in said step A, the catalytic thiol is benzyl mercaptan.

4. A method as described in Claim 2 wherein, in said step A, the catalytic thiol is a conjugated thiol selected from the group consisting of thiophenol, 1-thio-2-nitrophenol, 2-thio-benzoic acid, 2-thio-pyridine, 4-thio-2-pyridinecarboxylic acid, and 4-thio-2-nitro-pyridine.

5

10 5. A method as described in Claim 4 wherein, in said step A, the conjugated thiol is thiophenol.

15 6. An oligopeptide intermediate comprising:
a first oligopeptide segment having a C-terminal thioester,
a second oligopeptide segment having a N-terminal cysteine, and
a β -aminothioester linkage unit linking the C-terminal thioester and the N-terminal cysteine, said β -aminothioester linkage unit spontaneously rearranging intramolecularly to form an amide bond linking said first and second oligopeptides segments end to end.

20

7. A method for producing an oligopeptide having a C-terminal thioester, the method comprising the following steps:

5 Step A: providing a resin having a linker with an unoxidized thiol;

Step B: providing a Boc-amino acid succinimide ester; then

10 Step C: admixing the resin of said Step A and the Boc-amino acid succinimide ester of said Step B under reaction conditions for producing a Boc-amino thioester-resin; then

15 Step D: assembling an oligopeptide onto the Boc-amino thioester-resin by stepwise solid phase peptide synthesis; then

Step E: cleaving the Boc-amino thioester-resin of said Step D with HS for producing an oligopeptide having a C-terminal thiol; and then

20 Step F: converting the oligopeptide having a C-terminal thiol of said Step E to the oligopeptide having a C-terminal thioester.

Add
Al